REMARKS

I. Status of the claims

Claims 1-4, 7-16, 20-27, and 30-44 are pending. Claims 39-44 remain withdrawn and claims 5, 6, 17-19, 28, and 29 remain cancelled. Claims 1, 7, 16, and 27 have been amended in this response to address typographical errors identified by the examiner.

II. Rejection under 35 U.S.C. § 101

The examiner has rejected claims 16 and 20-26 under 35 U.S.C. § 101 because the claimed invention is alleged directed to non-statutory subject matter. In particular, the examiner notes that the claims are directed to computer readable media having instructions stored thereon which "...encompass both functional as well as non functional descriptive material." However, the examiner fails to give any indication of which instructions are deemed to be non functional descriptive material. Further, even if there is non functional descriptive material included in the claims, this does not preclude patentability under 35 U.S.C. § 101.

As noted in the United States Patent and Trademark Office OG Notices: 22 November 2005, Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility:

> *Nonfunctional descriptive material may be claimed in combination with other functional descriptive multi-media material on a computer-readable medium to provide the necessary functional and structural interrelationship to satisfy the requirements of 35 U.S.C. Sec. 101.* The presence of the claimed nonfunctional descriptive material is not necessarily determinative of nonstatutory subject matter. For example, a computer that recognizes a particular grouping of musical notes read from memory and upon recognizing that particular sequence, causes another defined series of notes to be played, defines a functional interrelationship among that data and the computing processes performed when utilizing that data, and as such is statutory because it implements a statutory process.

Emphasis supplied.

For the reasons noted above, even assuming, *arguendo*, that the claims include non functional descriptive material along with functional instructions, as noted by the examiner, the claims are directed to statutory subject matter. For these reasons, the rejection based on 35 U.S.C. § 101 should be withdrawn.

III. Written Description Rejection

The examiner has rejected claims 1-4, 7-16, 20-27, and 30-38 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The examiner states that the term "conjugate caps" is not sufficiently described in the specification such that one skilled in the art would be apprised of the structure intended. Applicants respectfully traverse this rejection.

In analyzing paragraphs 38-41 in the specification, the examiner concludes that the specification does not disclose or exemplify the conjugate (second cap member) that corresponds to the first cap member. According to the examiner, one skilled in the art would not know what relationship caps must have to each other to be considered conjugated. The examiner acknowledges that the specification states that a cap should mimic as much as possible the effect of the original molecule part being cut away from the remaining fragment. See paragraph 40. Yet the examiner does not understand how this accomplished.

Applicants direct the examiner's attention to paragraphs 40-42, which should be analyzed in view of the figures, particularly Figure 1. Figure 1 exemplifies a graphical representation of an extended tripeptide showing the locations of the decomposition points where conjugated caps are introduced. See paragraph 12. Paragraphs 40-41 discuss how one skilled in the art approaches the application of the caps to the tripeptide exemplified in Figure 1.

As discussed in paragraph 40, the first cap on the A2 molecular fragment in Figure 1, C^1_{ap}, should represent the electronic effect of everything to the right side of the first decomposition point. Looking at Figure 1, the first decomposition point occurs between the nitrogen atom of the nA1 fragment that is bonded to the carbon atom of the A2 fragment. Everything to the right side of the first decomposition points in Figure 1 is represented as $C_\alpha H(R_2)CONHC_\alpha H(R_3)COO^-$. One skilled in the art could therefore choose $C_\alpha H(R_2)CONH_2$ as a cap to mimic the functionality present in the larger molecule fragment. In this scenario, C^1_{ap} is thus $C_\alpha H(R_2)CONH_2$.

As further discussed in paragraph 40, C^{1*}_{ap}, the conjugate cap to C^1_{ap}, should closely represent the electronic effect of nA1 on the A2 unit; in other words, everything to the left of the first decomposition point. nA1 is represented in Figure 1 as $H_3N^+C_\alpha H(R_1)CONH$. One skilled in the art could therefore choose NH_2 (NH_3^+) to mimic the amine functionality present in the

larger molecular fragment. (Protons can be removed or added to the caps, as appreciated by those of skill in the art, to represent the caps in either a charged state or a neutral state.) Thus, in this scenario, C^{1*}_{ap} is NH_2. Alternatively, one skilled in the art could choose a larger cap such as $C_\alpha H_2(R_1)CONH$ to capture the amide functionality of the molecular fragment. However, for the purposes of this explanation, C^{1*}_{ap} will represent NH_2.

As discussed in paragraph 42, after a molecule has been decomposed and capped with conjugate caps to create a plurality of molecular portions, the molecular portions may be used to measure intermolecular interaction energy. In the example discussed above, there are two molecular portions: the nA1 molecular fragment that has been capped with $C_\alpha H(R_2)CONH_2$, i.e. $H_3N^+C_\alpha H(R_1)CONH\ C_\alpha H(R_2)CONH_2$, and the molecular fragment consisting of A2 and A3c that has been capped with NH_2, i.e. $H_2NC_\alpha H(R_2)NH\ C_\alpha H(R_3)COO^-$. The caps are coupled to form conjugated caps. In this case, the $C_\alpha H(R_2)CONH_2$ cap is coupled with the NH_2 cap to form $H_2N\ C_\alpha H(R_2)CONH_2$. See paragraph 64 for an additional discussion of the coupling process.

A second molecular is introduced, and the interaction energies are determined between each molecular portion ($H_3N^+C_\alpha H(R_1)CONH\ C_\alpha H(R_2)CONH_2$ and $H_2NC_\alpha H(R_2)NH\ C_\alpha H(R_3)COO^-$) and the second molecule, and between the conjugated caps ($H_2N\ C_\alpha H(R_2)CONH_2$) and the second molecule. Each cap of the conjugated caps is thus part of two interaction energy equations. When calculating an intermolecular interaction energy, the interaction energy of conjugated caps is discounted so that an accurate determination of the intermolecular interaction energy between two molecules can be determined. This allows for a skilled artisan to choose various caps, provided the cap reasonably mimics the molecular fragment that it is substituted for. It does not matter if different skilled artisans were to choose different caps, as the conjugate caps, regardless of which cap is used, will be accounted for in the total intermolecular interaction energy calculation.

As can be seen in the exemplified tripeptide shown in Figure 1 and discussed in paragraphs 40-42 of the specification, one skilled in the art would understand how conjugate caps are determined and the relationship the conjugate caps have with each other and to the first molecule in the context of determining the total intermolecular interaction energy.

Applicants provide the above-described model as a simple example using a molecule that contains one decomposition point. As shown in Figure 1, the peptide could contain two (or

more) decomposition points. For molecules containing additional decomposition points, a skilled artisan would simply apply the process discussed above to each molecular fragment.

Another example of how the conjugate caps may be added to a molecule is provided in the attached Addendum. The Addendum was prepared by Dr. John Z. H. Zhang, lead inventor on this application and Professor of Chemistry at New York University. The Addendum illustrates another example of how a molecule can be decomposed into molecular fragments, the capping of the molecule with a small molecular species (a cap), and the coupling of caps to form conjugate caps. If necessary, this Addendum can be resubmitted to the Office in the form a declaration to provide further evidence of how one skilled in the art would understand the disclosure in the patent application.

In view of the above remarks, Applicants respectfully request that the examiner withdraw this rejection under 35 U.S.C. § 112, first paragraph.

IV. New Matter Rejection

The examiner has rejected claims 1-4, 7-16, 20-27, and 30-38 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The examiner states that this is a new matter rejection based upon the amendment introduced during the previous response. Applicants respectfully traverse this rejection.

The examiner states that "the disclosure as originally filed does not provide written support for the limitation of coupling each pair of caps." Yet, in the very next sentence, the examiner stipulates that "the specification does disclose on [0064] the formation of a coupled cap by coupling conjugate caps."

Applicants respectfully submit that an original disclosure stating that "the conjugate caps can then be coupled," as disclosed in paragraph 64, provides more than adequate support for a claim limitation that recites the "coupling [of] each pair of caps," as recited in claims 1, 16, and 27. It is well established in case law that an *in haec verba* recitation is not necessary to comply with the written description requirement. *See In re Smythe*, 178 USPQ 279 (CCPA 1973); *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961 (Fed. Cir. 1997).

In this case, Applicants have done nothing more than incorporate into claim format the disclosure in paragraph 64 relating to the pairing of the caps. Amending the claims in this

manner is completely permissible under U.S. patent laws. Accordingly, Applicants respectfully request that the examiner withdraw this rejection under 35 U.S.C. § 112, first paragraph.

V. Rejection under 35 U.S.C. § 112, second paragraph

The examiner has rejected claims 1, 16, and 27 under 35 U.S.C. § 112, second paragraph based on insufficient antecedent basis for the term "the second molecule." Applicants have amended these claims to introduce the first recitation of the second molecule with the article "a."

The examiner has also rejected claim 7 under 35 U.S.C. § 112, second paragraph based on insufficient antecedent basis for the term "the molecular portion." Applicants have amended claim 7 to change this term to "the molecular portions," per the examiner's suggestion.

In view of these amendments, Applicants respectfully request that the examiner withdraw the rejections under 35 U.S.C. § 112, second paragraph.

VI. Conclusion

Except for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 19-2380. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. §1.136(a)(3).

Respectfully submitted,

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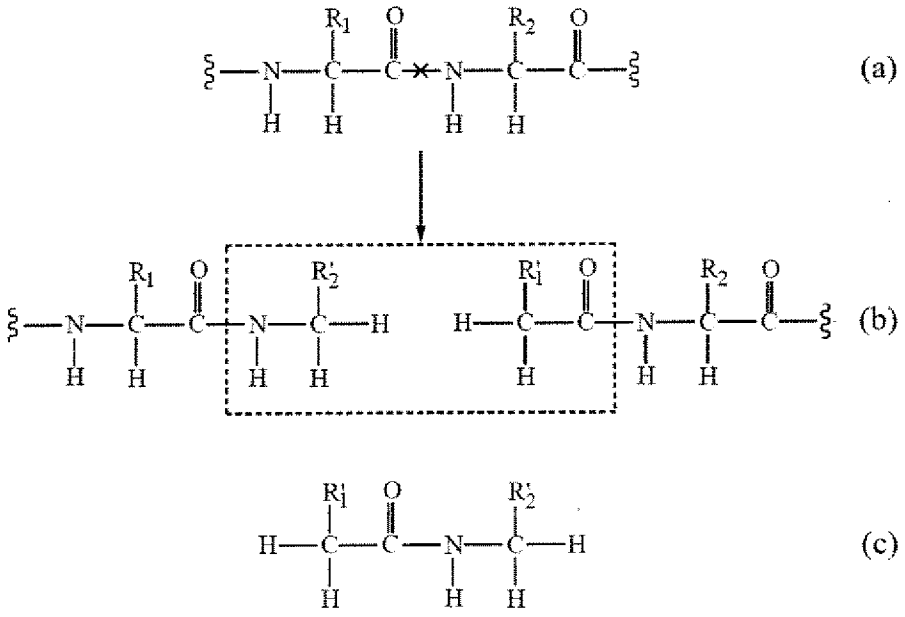
Addendum

In the Molecular Fragmentation with Conjugate Caps (MFCC) approach, the decomposition of the molecule into fragments may be accomplished through cutting of certain covalent bonds of the molecule. For example, if a molecule P in question (such as a protein or a polymeric molecule in general) is expressed as A-B, where the A and B portions of the P molecule are connected by covalent bonds, the MFCC procedure will decompose the P molecule into three smaller molecular species: A-c, B-c*, and c*-c (demonstrated in the figure). The c is a small molecular entity or chemical group (usually a radical) and c* is another small molecular entity. The c and c* are coupled or fused (covalently bond) to form a new small molecular species c*-c. The figure below illustrates this process.



Thus, for every cut of a covalent bond, there will be a pair of caps (c and c*) that cap, respectively, the two fragments resulting from the cutting. Because they appear together in pairs and are also fused or coupled to form a new molecular species, they are referred to as conjugate caps. This definition of conjugate caps is more general than acid/base definition and many chemical groups (usually radicals) can be included. The composition of the cap is quite general and can be either charged or uncharged. However, they are normally chosen to mimic the neighboring chemical environment of the fragment.